II. RESPONSE TO OFFICIAL ACTION

A. Status of the Claims

The status of several claims listed at page 2 of the Action is unclear to the Applicants as the listing of claims rejected under 35 U.S.C. 112, first paragraph does not appear to fully reflect the amendments requested in the previous Response. Consideration of the amended claims is respectfully requested. Applicants believe that claims 1, 5-7, 10, 11, 22, 26, 28, 30, 32, 34, 36, 38, 40-43, 45-50, 107, 111, 113, 115, 117 were pending in the case at the time of the present Action. Claims previously withdrawn from consideration have been canceled herein. Claims 1-9, 11-21, 23-27, 29-31, 33, 35, 37, 39, 44, 51-106, 108-110, 112, 114, 116, 118-120 have been canceled in total herein without prejudice, claims 10, 22, 43, 46, 107 and 113 amended, and claims 121-125 added. Support for the amendment of claims 1, 10, 11, 22, and 107 is found in the specification, at least, at page 14, lines 21-31, and in Example 9. Support for the new claims is found in claim 10. No new matter is added by the amendments. Claims 10, 22, 28, 32, 34, 36, 38, 40-43, 45-50, 107, 111, 113, 115, 117 and 121-125 are now believed pending in the case and are presented for reconsideration.

B. Rejections Under 35 U.S.C. §112, First Paragraph- Written Description

The Action rejects claims 1-2, 5, 10-11, 22-23, 26, 28, 30, 32, 34, 36, 38, 40-50, 76, 78, 82, 84, 86, 88, 107, 108, 111, 113, 115, and 117 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Applicants initially request clarification as to which claims are covered by this rejection, as noted above. Applicants respectfully traverse the rejection.

The current claims are fully supported by a written description in the specification demonstrating possession of the invention. In particular, the current claims define a scope of subject matter described in the specification. For example, the claims require sequences encoding the polypeptide of SEQ ID NO:5 or having at least 80% sequence identity or hybridizing under stringent conditions to SEQ ID NO:4. Applicants were in full possession of this subject matter based on the description of SEQ ID NOs:4 and 5 as it is well settled that an Applicant need not limit the claims to that subject matter having *ipsis verbis* description. *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (stating that the written description requirement does not require an applicant to "describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (citations omitted)). Further, written description must be reviewed from the perspective of one of skill in the art at the time the application is filed. *Wang Labs., Inc. v. Toshiba Corp.*, 993 F.2d 858, 863 (Fed. Cir. 1993).

In the instant case it was routine in the art as of the filing date to make silent changes to a given polypeptide while retaining activity, and these changes were described in the specification. For example, changes can be made to coding sequence without even changing the polypeptide sequence by altering codon usage. The Detailed Description of the Invention also describes the use of techniques for changing amino acids of a polypeptide while retaining or even improving enzymatic activity. For example, it is explained that conservative amino acid substitutions can be made by substitution of a residue with another having like characteristics. One criteria described is the hydropathic index of amino acids. It is noted that the relative hydropathic character of amino acids contributes to the secondary structure of the resultant protein and thus interaction of the protein with molecules such as enzymes, substrates, receptors, DNA,

antibodies, antigens, etc. Based on hydrophobicity and charge characteristics, each amino acid has been assigned a hydropathic index and these are given in the specification. Those amino acids sharing a similar score may be selected and substituted for one another based on the known hydropathic indices.

It is also explained in the specification that like amino acids can be substituted based on hydrophilicity, and that this is explained in U. S. Patent No. 4,554,101. Values for assessing hydrophilicity have been assigned and can be used for selecting an amino acid for substitution, as described in the specification. It is also known that amino acid substitutions can be based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, etc. Use of these changes is also described, as further outlined in the response to the enablement rejection below. There is therefore no basis in law or science to attempt to limit Applicants to any less than what is being claimed.

With respect to the assertion at page 3, middle paragraph of the Action that (increased) formation of sterol esters in transformed cells is shown only with respect to SEQ ID NO:6 and SEQ ID NO:8, Applicants note that the current claims are directed to SEQ ID Nos:4 and 5 and related sequences and that Example 7 shows that such an LCAT2 gene was expressed in plants yielding a significant increase in the oil level in seed from T2 plants. Fig. 5 and Table 2. Applicants also note that LCAT2 is described in the cited Noiriel reference as possessing sterol acyltransferase activity (see p.3757 2nd col; and refs 48a, 48b cited therein). Applicants respectfully submit that the Noiriel reference does not in any way teach that the presently claimed LCAT2 and related sequences lack acyltransferase activity. On the contrary, Noiriel *et al.* clearly state that LCAT2 is a sterol acyltransferase. Additionally, the present specification, at page 49, lines 5-17; figure 5; and table 2, pages 50-51 describes use of LCAT2, encoded by SEQ

ID NO:4, in creating transgenic plants with increased oil content. This is also noted by the Action at page 5, fourth paragraph. In view of the foregoing and currently claimed subject matter, Applicants submit that the rejection is now moot and respectfully request that it be withdrawn.

C. **Rejections Under 35 U.S.C. §112, first paragraph-enablement**

The Action rejects claims 1-2, 5, 10-11, 22-23, 26, 28, 30, 32, 34, 36, 38, 40-50, 76, 78, 82, 84, 86, 88, 107, 108, 111, 113, 115, and 117 under 35 U.S.C. §112, first paragraph, as lacking enablement. Applicants initially request clarification as to which claims are covered by this rejection, as noted above. Applicants respectfully traverse

Applicants note that the full scope of currently claimed subject matter is enabled. While the claims, in addition to covering nucleic acids encoding the polypeptide sequence of SEQ ID NO:5 and comprising SEQ ID NO:4, cover sequences that hybridize with these sequences under specified stringent conditions or have at least 80% sequence identity to SEQ ID NO: 4, at most routine experimentation would be required for one of skill in the art to make and use the full scope of claimed subject matter. For example, it is routine for one of skill in the art to create sequence variants comprising silent nucleic acid mutations or those leading to conservative amino acid changes such that the activity of the encoded polypeptide is maintained. Creation of sequence variants only requires routine substitution of the starting nucleic acid molecules, which is fully described in the specification and well known in the art.

The Detailed Description of the Invention, in particular, describes the techniques one of skill in the art would use to change amino acids of a polypeptide encoded by any of the claimed nucleic acids while retaining or even improving enzymatic activity. For example, it is explained

in the Detailed Description that conservative amino acid substitutions can be made by substitution of a residue with another having like characteristics. It is explained that one criteria that may be used in this regard is the hydropathic index of amino acids and that the significance of hydropathic amino acid index in conferring biological function of a protein has been discussed by Kyte and Doolittle (*J. Mol.Biol.*, 157: 105-132, 1982). It is noted that the relative hydropathic character of amino acids contributes to the secondary structure of the resultant protein and thus interaction of the protein with molecules such as enzymes, substrates, receptors, DNA, antibodies, antigens, etc. Based on hydrophobicity and charge characteristics, each amino acid has been assigned a hydropathic index and these are given in the specification. Those amino acids sharing a similar score may be selected and substituted for one another based on the known hydropathic indices.

It is also explained in the specification that like amino acids can be substituted based on hydrophilicity, and that this is illustrated in U. S. Patent No. 4,554,101. Values for assessing hydrophilicity have also been assigned and can be used for selecting an amino acid for substitution, as described in the specification. It is also known that amino acid substitutions can be based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, etc. In this regard the specification explains that amino acids can be divided into the following four groups: (1) acidic amino acids; (2) basic amino acids; (3) neutral polar amino acids; and (4) neutral nonpolar amino acids, and that representative amino acids within these various groups include, but are not limited to: (1) acidic (negatively charged) amino acids such as aspartic acid and glutamic acid; (2) basic (positively charged) amino acids such as arginine, histidine, and lysine; (3) neutral polar amino acids such as glycine, serine, threonine, cysteine, cystine, tyrosine, asparagine, and glutamine; and (4)

neutral non-polar amino acids such as alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine. Similarities within these groups can also be used to substitute an amino acid.

The specification therefore fully enables the claim scope based on the provision of SEQ ID NO:4 and SEQ ID NO:5. While some routine mutagenesis may be required to generate sequence variants, this would not be undue because the techniques that would be used are targeted, well known in the art, and fully described in the specification. The biological activity of any given sequence generated could routinely be confirmed by the transformation of plants with plant transformation vectors comprising the sequences followed by measurement of seed oil quantity and/or quality using the methodology of working Examples 4, 6 and 7.

Regarding claims covering transgenic plants, the experiments in the specification, e.g. Example 4, describe the creation of transgenic plants comprising an LCAT2 transgene. Further, Example 7 shows that, as demonstrated in Figure 5 and Table 2, there was a significant increase in the oil level in seed from T2 plants expressing the LCAT2 gene. This increase in oil was seen in plants when LCAT2 was driven by either the 35S constitutive promoter or the seed-specific napin promoter. These plants are representative of the claimed sequences, as the claims are limited to sequences of close structural relation, as demonstrated above. Again, it was routine as of the filing date to make conservative modifications altering polypeptides without destroying enzymatic activity and the working examples show the corresponding activity and phenotypic effect.

The Action also asserts that a likely candidate for lecithin:cholesterol acyltransferase showed phospholipase A1 activity (Noiriel *et al.*), and thus the specification is not enabling for any lecithin:cholesterol acyltransferase-like sequence to be confirmed as an acyltransferase. In

response, Applicants first note that the present claims relate to the nucleic acid and amino acid sequences of SEQ ID NO:4-5, *i.e.*, for LCAT2, rather than the AtLCAT3 protein described by Noiriel as possessing phospholipase activity. The working examples further show activity for this sequence. In addition, the LCAT2 and LCAT3 genes are structurally distinct, sharing less than approximately 48% identity at the DNA level and 22% identity at the protein level (*e.g.* when SEQ ID NO:4 is compared to SEQ ID NO:6). Thus, no conclusions can be made as suggested with respect to LCAT2-like sequences.

In sum, Applicants have affirmatively demonstrated enablement of the claims and no basis to doubt the enablement has been provided. Removal of the rejection is thus respectfully requested.

D. Rejections Under 35 U.S.C. §102(a)

The Action rejects claims 1, 5-7, 10-11, 22, 26, 28, 30, 32, 34, 36, 38, and 40 under 35 U.S.C. 102(a) as being anticipated by Federspiel *et al.* Applicants respectfully traverse.

Applicants first note that the current claims are directed to coding sequences operably linked to a heterologous promoter functional in plants. This elements has not been shown in the Action and thus the claims cannot be anticipated. It is further noted in this regard that the Federspiel LCAT2 protein sequence as found in GenBank AAD10668, accession version AC003027.1 from the TIGR BAC F21M11 genomic clone, was annotated as a "hypothetical protein", without assigned function, at least as late as October 30, 2002, which date is well after the priority date of the present application. Federspiel *et al.* did not teach that this sequence encoded an LCAT-like protein as of the filing date of the present application. Knowledge of the function of this hypothetical protein sequence was thus not of "common knowledge" as outlined

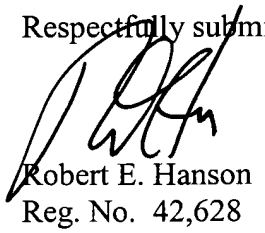
by the citation at page 8 of the Action (*Continental Can Co. USA v. Monsanto Co.*, 948 F. 2d 264, 1268 20 USPQ at 1749-50 (Fed. Cir. 1991). Finally, the specification at page 31, lines 24-30, does not state that the sequences are identical, but rather that an LCAT2 sequence could be identified within AC003027 by BLAST search. It is clear that AC003027, comprising multiple genes and more than 119 KB of sequence from a genomic clone, can not be an LCAT2 sequence *per se*.

Because every element of the presently amended claims is not present in the reference, the claims are not anticipated by Federspiel. M.P.E.P. § 2142. In view of the above, and the amendments to the claims, Applicants respectfully request that the rejection be removed.

E. Conclusion

In light of the foregoing, Applicants submit that the case is in condition for allowance, and an early indication to that effect is earnestly solicited. The examiner is invited to contact the undersigned (512)536-3085 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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